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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/161,680	09/28/1998	UWE BORNSCHEUER	48429	7944

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/161,680	BORNSCHEUER ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[2] Claims 12-19 are pending in the application.

[3] Applicant's amendment to the claims, filed on 11/3/2005, in response to the Decision on Appeal, mailed on 9/29/2005, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims. It is noted that the amendment filed on 11/3/2005 fails to provide a list of all claims, namely claims 1-11. *Applicant is reminded of the revised amendment practice of 37 CFR 1.121.*

Specification

[4] The amendments to the specification filed on 4/15/2003, 9/16/2003, and 11/6/2003 are objected to under 35 U.S.C. 132(a) because they introduce new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is cited in the Decision on Appeal mailed on 9/29/2005 at pp. 12-14. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112, Second Paragraph

[5] Claim(s) 12-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] The last line three lines of claim 12 (claims 13-19 dependent thereon) recite "the alteration in substrate specificity leads to a stereoselective enzymatic activity." Solomon in "Fundamentals of Organic Chemistry" (John Wiley and Sons, New York, 1990) teaches "[t]he enzyme-catalyzed reaction is said to be stereoselective" (p. 167, bottom). Thus, the term "stereoselective" in the phrase "the alteration in the substrate specificity leads to a stereoselective enzymatic activity" does not modify or limit the term "enzymatic activity" because according to Solomon, *any* enzymatic reaction is – by definition – stereoselective. In other words, in view of the teaching of Solomon, the term "stereoselective" for the purpose of describing or modifying an "enzymatic activity" is redundant. As such, it is unclear as to the limitation imparted by the term "the alteration in substrate specificity leads to a stereoselective enzymatic activity." Consequently, it is unclear as to how one is to interpret the claim. For example, is the phrase "the alteration in substrate specificity leads to a stereoselective enzymatic activity" meant to indicate that the enzyme had no activity prior to mutation? If the unmodified enzyme has activity, how does alteration "lead[] to" stereoselective enzyme activity, *i.e.,* is it a direct effect of alteration or an indirect effect? It is suggested that applicant clarify the meaning of the claim. It is noted that the specification fails to define the term "stereoselective" and has been interpreted according to its art-recognized as "a reaction that yields exclusively (or predominantly) only one of a set of stereoisomers" (Solomon, p. 167, bottom).

[b] Claims 14 and 16-18 recite the limitations "an amidase," "an ether hydrolase," "a peroxidase," and "a glycosidase," respectively. There is insufficient antecedent basis for these limitations in claim 12. It is suggested that applicant provide antecedent basis for these limitations in the claim(s).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[6] In the Decision on Appeal mailed on 9/29/2005, the Board stated that the examiner "may wish to consider whether the claims are patentable under 35 U.S.C. § 103 in view of Greener alone or in combination with another reference." Claim(s) 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greener et al. (*Methods Mol Biol* 57:375-385, cited on the 11/30/1999 Form PTO-1449) in view of Short et al. (US Patent 5,830,696). The claims are drawn to a method for altering the substrate specificity of a lipase, amidase, nitrilase, ether hydrolase, peroxidase, or glycosidase using an XL-1 Red *E. coli* strain for DNA mutagenesis, transferring the resulting mutant DNA into a microorganism and selecting microorganisms that show stereoselective enzyme activity in or on a selection medium comprising an enzyme substrate that makes it possible to recognize the altered substrate specificity.

Greener et al. teaches development of "a new strain of *E. coli* called XL1-Red" that can generate "a family of single-point mutations randomly within a cloned gene of interest...with just overnight growth" (p. 375, middle). Greener et al. teaches methods of using XL1-Red to mutate an encoding nucleic acid to obtain a desired variant (pp. 375-378). Greener et al. demonstrates the method by obtaining variants of beta-lactamase and alkaline phosphatase (pp. 381-384), by selecting desired variants by transferring the mutated DNA sequence into a strain that lacks the enzyme activity, incubating this strain in the presence of a selection medium and selecting those transformants that have increased or decreased activity "p. 383, paragraph 8). Greener et al. does not teach selecting transformants in or on a selection medium comprising an enzyme substrate that makes it possible to recognize *stereoselective* enzyme activity.

Short et al. teaches a method for mutating an enzyme using the XL-1 Red strain of *E. coli* (column 5, lines 26-32) and screening the clones containing the mutated DNA in a phenotypic assay to determine their activity (column 5, lines 54-56). Short teaches a "representative list" of enzymes that may be mutagenized by the disclosed method, including (in relevant part) lipases, esterases, glycosidases, epoxide hydrolases (which are ether hydrolases), peroxidases, nitrilases, and amidases (columns 6-7). Short et al. teaches that the activity of enzyme that can be mutated according to the method includes altered substrate specificity, including *inter alia,* altered substrate stereoselectivity. Short et al. demonstrates the method by altering the activity of alkaline phosphatase and beta-galactosidase using XL1-Red and testing transformants on an appropriate medium for those that show the desired activity.

Therefore, at the time of the invention it would have been obvious to one of ordinary skill in the art to combine the teachings of Greener et al. and Short et al. for a method for altering the substrate specificity of a lipase, amidase, nitrilase, ether hydrolase, peroxidase, or glycosidase using an XL-1 Red *E. coli* strain for DNA mutagenesis, transferring the resulting mutant DNA into a microorganism and selecting microorganisms that show altered substrate specificity in or on a selection medium comprising an appropriate enzyme substrate. One would have been motivated to alter the substrate specificity of a lipase, amidase, nitrilase, ether hydrolase, peroxidase, or glycosidase because of the teachings of Short et al. as described above. One would have a reasonable expectation of success for the method described above because of the results of Greener et al. and Short et al. and in view of applicant's remarks in the 11/3/2005 response that "the experimentation required for claims 12-19 would be a routine matter for the skilled artisan" (p. 5, top). Therefore, claims 12-18, drawn to the method described above would have been obvious to one of ordinary skill in the art at the time of the invention.

[7] Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Greener et al. in view of Short et al. as applied to claims 12-18 above and further in view of van der Kaay (*Biochem J* 312:907-910). Claim 19 limits claim 12 to a phytase.

Greener et al. and Short et al. disclose the teachings as described above. Neither Greener et al. nor Short et al. discloses mutagenesis of phytase.

Van der Kaay et al. teaches "[i]nvestigations of the routes of InsP6 synthesis would be helped by the availability of enzymes that dephosphorylate InsP6 in a position-

specific order" and that "[t]his would allow us to follow the kinetics of incorporation and release of radioactive phosphate at each position of the molecule after pulse-labelling cells with [32P]Pi" in order to establish the metabolic routes of many compounds *in vivo* (p. 907, left column, middle).

Therefore, at the time of the invention it would have been obvious to one of ordinary skill in the art to combine the teachings of Greener et al., Short et al., and van der Kaay for a method for altering the substrate specificity of a phytase using an XL-1 Red *E. coli* strain for DNA mutagenesis, transferring the resulting mutant DNA into a microorganism and selecting microorganisms that show altered substrate specificity in or on a selection medium comprising an appropriate enzyme substrate. One would have been motivated to alter the substrate specificity of a phytase in order to obtain phytase enzymes that dephosphorylate InsP6 in a position-specific order in order to establish metabolic routes of compounds *in vivo* as taught by van der Kaay. One would have a reasonable expectation of success for the method described above because of the results of Greener et al., Short et al., and van der Kaay and in view of applicant's remarks in the 11/3/2005 response that "the experimentation required for claims 12-19 would be a routine matter for the skilled artisan" (p. 5, top). Therefore, claim 19, drawn to the method described above would have been obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

[8] Status of the claims:

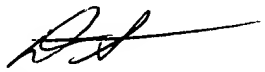
Claims 12-19 are pending.

Claims 12-19 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs, 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656